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(DOCUMENT SECTION)

Enc. 4

ITEM No. 24  
FILE No. XXVI-73

COPY No. 121

CLASSIFICATION CHANGED  
TO **UNCLASSIFIED**  
AUTH Sec I Vol I J10A Acc List  
DATE 26 June 1947  
SECURITY OFFICER  
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INSECTICIDES, INSECT REPELLENTS,  
RODENTICIDES AND FUNGICIDES

I.G. FARBENINDUSTRIE A.G.,  
ELBERFELD AND LEVERHUSEN

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INSECTICIDES, INSECT REPELLENTS, RODENTICIDES AND FUNGICIDES

OF

I. G. FARBENINDUSTRIE A. G.  
ELBERFELD AND LEVERKUSEN, GERMANY

19-30 May 1945

Reported by

Dr. STANLEY A. HALL, U.S. Civilian  
Office of the Chief Surgeon, Hq. USFET

CIOS Target Nos. 24/1, 24/3  
Medical

COMBINED INTELLIGENCE OBJECTIVES SUB-COMMITTEE  
G-2 Division, SHAEF (Rear) APO 413

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TABLE OF CONTENTS

<u>Subject</u>	<u>Page No.</u>
I. INTRODUCTION.....	3
II. INSECTICIDES.....	5
a. "ME 1700", "DDD" or 1,1-dichloro-2,2 bis(p-chlorophenyl)-ethane.....	5
b. "ME 1748", "Gix", "Fluorgesarol" or 1-trichloro-2,2-bis(p-chlorophenyl)- ethane.....	6
c. "Lauseto-neu" or phenylchloromethyl sulfone and p-chlorophenylchloro- methyl sulfone.....	7
d. Compounds prepared by Dr. Meiser showing insecticidal activity.....	9
e. p-chlorophenyl-trichloromethyl carbinol.....	9
f. "Bladan" or hexaethyl ester of tetra- phosphoric acid.....	10
III. MOSQUITO REPELLENTS.....	10
a. Testing at Elberfeld.....	10
b. "Presinol" or "Mipax".....	11
c. Effect of calcium chloride to enhance repellency.....	11
d. Simplified "Mipax" formula.....	12
e. Esters of phthalic acid.....	12
f. "Repellent 50/181" or trichloroace- tylchloroethylamide.....	12
g. Impregnation of cloth with repellents Comment on repellent testing.....	12 13
IV. RODENTICIDES.....	13
a. "Castrix" or 2-chloro-4-methyl-6- dimethylaminopyridine.....	13
b. p-dimethylaminobenzene diazonium sulfonic acid, sodium salt.....	13
V. FUNGICIDES.....	14
VI. A COMPOUND FOR TESTING SEED GERMINATION..	16
a. Triphenyltetrazolium chloride.....	16
Appendix 1. "Preparation of 1,1-dichloro-2,2- bis(p-chlorophenyl)-ethane".....	17
" 2. "Substances tested against body lice". Dr. Stötter.....	19
" 3. Results of testing repellents and mosquitocides. Dr. Mudrow.....	24
" 4. "Preparation of triphenyltetra- zolium chloride".....	45



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### I. INTRODUCTION

The undersigned, an investigator attached to the Medical Intelligence Branch, Office of the Chief Surgeon, was ordered to proceed by aircraft, on 19 May 1945 to Wiesbaden and thence to Elberfeld (Target 24/1) and Leverkusen (Target 24/3), Germany, for the purpose of investigating plants of the I. G. Farbenindustrie, A. G. at these two locations. The subjects covered in this investigation comprise primarily insecticides and mosquito repellents, but also include rodenticides, fungicides and one organic miscellaneous chemical.

On arrival at Elberfeld the undersigned joined a team composed of Drs. Rice, Kleiderer, and Conquest who were investigating other phases of the research of the I. G. Farbenindustrie. Since much of the research at the Elberfeld and Leverkusen Laboratories has been closely interlocking, the results of investigations of these two places have been combined and are presented in this single report.

The German scientists at the I. G. Farbenindustrie have had an active interest in the field of insecticides and insect-repellents, but have carried out research on a considerably smaller scale than we have in the United States. In general, it can be said that the German advances are behind our own in this field.

It is especially difficult to evaluate the results of their entomological testing since it has been carried out, for the most part, in a rather haphazard fashion, not at all conducive to drawing reliable conclusions.

It is, therefore, difficult to evaluate their claims short of subjecting them to our own experimental tests. This applies to some of their chemical as well as to all of their entomological work. They claim, for example, that the insecticide which we know as DDD (their designation, ME 1700) or 1,1-dichloro-2,2-bis(p-chlorophenyl)-ethane can be produced in good yield from ethanol, chlorine and chlorobenzene by the Bayer Condensation without the formation of any DDT in the reaction. If our own experiments should confirm this,



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then this information would be of value to us, since we already know that DDD is as effective as a larvicide as DDT and presumably the DDD could be produced by this method more cheaply and not subject to the Geigy patent.

The German claims as to the superior insecticidal action of their ME 1748 ("Gix" or "Fluorgesarol") 1-trichloro-2,2-bis(p-fluorophenyl)-ethane, in comparison to DDT, are not clearly supported by their meager and inadequate tests against houseflies. Moreover, the Germans who tested it differ sharply among themselves as to their conclusions.

Likewise, the German claims of a superior insecticide against body lice and bedbugs called "Lauseto-neu" (a mixture of phenyl-chloromethyl sulfone and p-chlorophenyl chloromethyl sulfone) must be treated with skepticism until confirmed by sound testing methods.

Their testing of mosquito repellents was especially poor and inadequate.

It may prove that their repellent designated as 50/181 or trichloroacetylchlorethylamide will hold some value for us; but, in general, the Germans have lagged far behind us in the development of mosquito repellents.

"Bladan" or the hexaethyl ester of tetraphosphoric acid is an insecticide claimed to be an excellent substitute for nicotine for use against aphids.

Two organic fungicides were turned up which may have some value to us.

Two new organic rodenticides were uncovered which may prove of value.

Finally, a new non-toxic organic compound for testing the germination of seeds was uncovered. This may be of use to seed specialists.



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II. INSECTICIDES

1. ME 1700.

a. At Elberfeld.

1,1-Dichloro-2,2-bis(p-chlorophenyl)-ethane, known as "DDD" in the United States and designated as ME 1700 at Elberfeld, was prepared by Dr. Meiser. Of the DDT analogs (approximately 50) made by Meiser, the best from the standpoint of both cost and insecticidal activity as ME 1700 or DDD. That its insecticidal properties approach those of DDT against certain insects is not new since the Bureau of Entomology and Plant Quarantine of the U. S. Department of Agriculture has reported similar findings. Only one other analog of DDT prepared by Dr. Meiser, namely, 1-trichloro-2,2-bis(p-fluorophenyl)-ethane or "Gix" possesses the activity of DDT. DDD or ME 1700 is less toxic to warm-blooded animals than DDT according to a statement made by Dr. Schönhöfer.

Dr. Meiser prepared DDD by passing chlorine into ethanol (96%) at a reaction temperature of 25-30°C. The products formed are  $\text{Cl}_2\text{CHCH}(\text{OC}_2\text{H}_5)_2$ ,  $\text{Cl}_2\text{CHCHCl}(\text{OC}_2\text{H}_5)$ , and a small amount of  $\text{Cl}_2\text{CHCH}(\text{OH})_2$ . No chloral or chloral acetal is formed at this reaction temperature. The mixture of products from the chlorination of the alcohol is condensed directly, without further isolation, with chlorobenzene using oleum (Sp.G. 1.900 to 1.915) at 0 to 5°C. A good yield of DDD is obtained containing about 80% of the p,p' compound and about 17% of the o,p' compound which is quite analogous to the isomers obtained from the Bayer Condensation with chloral in commercial DDT manufacture. (See Appendix 1.).

Both Dr. Meiser and Dr. Schönhöfer have stated unequivocally that not a trace of chloral is formed when the first step of the reaction is carried out at the temperatures described. Hence no DDT is formed in the Bayer Condensation. If this statement is true, then the insecticide DDD would not be subject to the Geigy patent, and should also be simpler and cheaper to manufacture than DDT.



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b. At Leverkusen.

This compound (DDD or ME 1700) was not produced at Leverkusen according to Dr. Rüsche. Dr. Meiser at Elberfeld prepared it, but it was tested at Leverkusen. Dr. Bonrath at Leverkusen tested it against several species of caterpillars (Lepidoptera) and found it almost as effective as DDT. Against houseflies, mosquitoes (adults) and certain species of beetles it was as effective as DDT. Fed to rats and to cats, Dr. Bonrath found it no more toxic than DDT which he considers "non-toxic to warm-blooded animals".

On the other hand, Dr. Stötter and Dr. Laiboch tested this compound against moths, body lice and bedbugs in comparison with DDT and found DDD not sufficiently effective to warrant their further interest in it.

2. ME 1748

a. At Elberfeld.

1-trichloro-2,2-bis(p-fluorophenyl)-ethane, known as Fluorgesarol or "Gix" which is a liquid at room temperature, has been produced at Höchst. The fluorobenzene is obtained by diazotization of aniline in liquid HF. The insecticide is considerably more costly to produce than DDT. Dr. Meiser first prepared "Gix" in the laboratory, and Dr. Schönhöfer claims that it possesses a more rapid knock-down against flies than does DDT.

b. At Leverkusen.

"Gix" or Fluorgesarol was tested by Dr. Bonrath against houseflies. He impregnated filter paper with 0.5% "Gix" in acetone and placed the dried papers in dishes. Flies confined over the dishes were down after 30 minutes. He obtained the same results with DDT and found no essential difference between the action of "Gix" and of DDT against houseflies. Questioned as to why he did not use a Peet-Grady chamber with sub-lethal sprays of "Gix" and of DDT, he replied that these compounds are foot-poisons, (Fussgifte) and should not be used as fly-sprays.



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Drs. Räscher, Stötter, and Laiboch did not agree with Dr. Bonrath's conclusion that "Gix" is no better than DDT against houseflies. They said that "Gix" is faster-acting than DDT against flies. Dr. Laiboch, in running comparative tests, used a ventilated wooden box 20 x 25 cm square (inside dimensions). Sheets of white paper 20 x 25 cm were impregnated with 2%, 1% and  $\frac{1}{2}$ % of the substance to be tested. This impregnated paper was placed on the wall opposite to the window in the box. Twenty houseflies (2-3 weeks old, males and females) were introduced. The light shining on the paper through the window attracted all flies to walk on the paper. The flies were observed after 3 hours and counted:

<u>2%</u>		<u>1%</u>		<u><math>\frac{1}{2}</math>%</u>		<u>Number of Flies</u>
<u>Gix</u>	<u>DDT</u>	<u>Gix</u>	<u>DDT</u>	<u>Gix</u>	<u>DDT</u>	
17	5	9	...	1	...	Down
...	...	...	...	...	3	Badly affected
3	9	10	11	6	11	Affected
...	6	1	9	13	6	Slightly affected

The above is a typical run. Quite a number of such tests were made. From this type of testing it is difficult to see how one can conclude that "Gix" is superior to DDT. The compounds were not tried as sprays in a Peet-Grady chamber.

3. Lauseto-neu.

a. At Elberfeld.

This product, p-Cl-C<sub>6</sub>H<sub>4</sub>-SO<sub>2</sub>CH<sub>2</sub>Cl, made at Leverkusen is described by Dr. Schönhöfer as limited in its action to moths, mosquitoes and lice; but not effective against many insects including flies. Dr. Schönhöfer also stated that the chlorine in the benzene ring is not essential for insecticidal activity, i.e., C<sub>6</sub>H<sub>5</sub>-SO<sub>2</sub>CH<sub>2</sub>Cl is just as effective.

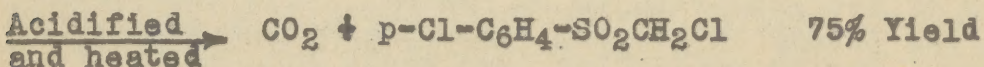
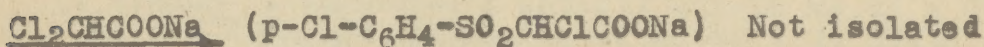
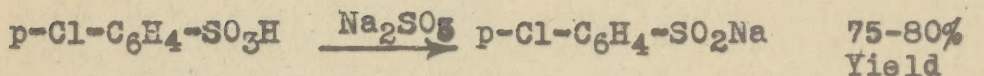
b. At Leverkusen.

Phenylchloromethyl sulfone, C<sub>6</sub>H<sub>5</sub>SO<sub>2</sub>CH<sub>2</sub>Cl, as well as p-chlorophenyl-chloromethyl sulfone, p-Cl-C<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>CH<sub>2</sub>Cl, are loosely termed "Lauseto-neu."



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Prof. Bayer described its preparation as follows:



Dr. Stötter has tested both the p-chlorophenyl sulfone and the phenyl sulfone against body lice and against bedbugs. He used pieces of cloth (in Petrie dishes) treated with a powder containing 0.3% and also 1% of active ingredient. Twenty insects were placed upon each piece of cloth and observed at definite time intervals under varying conditions to count the lice that were (1) unaffected, (2) slightly affected, (3) affected, (4) badly affected, and (5) dead. Compared in this manner to DDT, Dr. Stötter concluded that p-chlorophenylchloromethyl sulfone is 4 to 5 times more effective. The tests against bedbugs were run in much the same manner. Dr. Stötter stated that, while both the p-chlorophenyl sulfone and the phenyl sulfone were both much more effective than DDT against bedbugs, he found the phenyl sulfone better than the p-chlorophenyl sulfone against bedbugs. The reverse was found against body lice, i.e., the p-chlorophenyl sulfone was superior. (See Appendix 2).

Dr. Bonrath, who ran tests independently of Dr. Stötter against bedbugs (but not against body lice) stated that he found both the p-chlorophenyl sulfone and the phenyl sulfone about equally effective against bedbugs but definitely superior to DDT. Dr. Bonrath found both sulfones ineffective against caterpillars (4 species of Lepidoptera), beetles and houseflies.

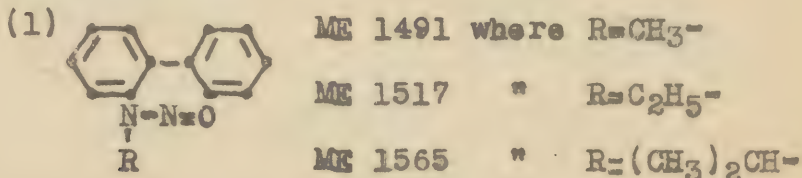
Dr. Rüsch stated that the sulfones (Lausetoneu) were used successfully against body lice and bedbugs in concentration camps. Tablets containing 44% of active ingredient compounded with bentonite and wetting agent were manufactured for making water emulsions of the preparation. Trichloroethylene has been found the best solvent for the sulfones.



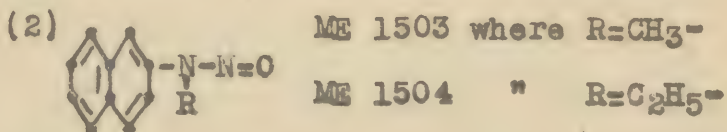
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4. Compounds Prepared by Dr. Meiser Showing Insecticidal Activity.

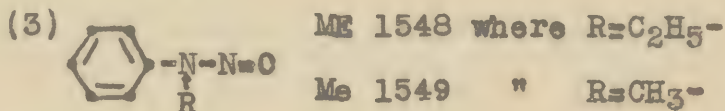
a. At Elberfeld.



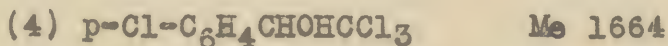
The above 3 compounds are described as fairly good stomach poisons, but are also toxic to warm-blooded animals. Higher homologs above isopropyl showed a rapid decrease in insecticidal activity.



The above 2 compounds are described as stomach poisons not so toxic to warm-blooded animals as the diphenyl analogs.



The above 2 compounds are also stomach poisons. No data given on their toxicity to warm-blooded animals.



The above compound is well known to us. Dr. Meiser stated that it has been found rather effective against flies.

b. At Leverkusen

p-Chlorophenyl-trichloromethyl carbinol (ME 1664) was tested by Dr. Bonrath who stated that it had no action against houseflies, but was effective only against adult mosquitoes. This is a flat contradiction of Dr. Meiser's statement that it was effective against houseflies.



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5. "Bladan"

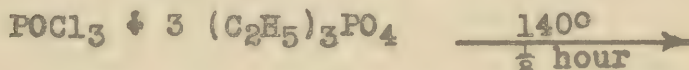
a. At Elberfeld.

Hexaethyl ester of tetraphosphoric acid.

$((C_2H_5O)_2PO)_3PO$ , known as "Bladan" was first prepared by Dr. Schrader.

b. At Leverkusen.

Dr. Podschus made it on a larger scale:



$3 C_2H_5Cl + ( (C_2H_5O)_2PO$  Yield almost  
quantitative.

It is a high-boiling liquid which does not distill without decomposition at atmos. press. The reaction product is used as an insecticide without any further purification.

It is bottled as 60% active ingredient plus 20% toluene plus 20% wetting agent. This concentrate is stirred into water (1 part in 1000 by vol.) giving an emulsion containing 0.06% active ester. The ester is almost completely hydrolyzed on standing in the water emulsion for 24 hours. Hence, the emulsion must be made up just before it is to be used as a spray. Dr. Bonrath claims that it is extremely effective against plant lice (aphids), and acts so rapidly that the subsequent hydrolysis to non-toxic phosphoric acid and alcohol is a definite advantage. No foliage injury has been found at concentrations up to 0.2%. According to Dr. Bonrath it is an excellent substitute for nicotine preparations against aphids.

III. MOSQUITO REPELLENTS

1. Testing Repellents at Elberfeld.

a. Comparatively little work has been done at Elberfeld in the field of mosquito repellents. What work has been done is not especially new nor was the testing done in a way to give reliable results.



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Approximately 50 substances and mixtures (mostly mixtures) were tested by Dr. Mudrow against Aedes aegypti and Culex fatigans. The latter species often could not be induced to bite the untreated arm of the subject.

b. "Presinol" or "Mipax".

This concoction contains the following ingredients:

100 g Cinnamyl alcohol	106 g Water
894 g Ethanol (96%)	1 g Melissen Oil
60 g. Calcium chloride (90-93%)	$\frac{1}{2}$ g Geraniol
40 g. Magnesium chloride	

The essential oils in this mixture, according to Dr. Dörr, who concocted it, are not necessary.

c. Effect of Calcium Chloride to Enhance Repellency.

Dr. Dörr stressed the action of calcium chloride in extending the repellent time of substances possessing repellency such as cinnamyl alcohol, coumarin, esters of phthalic acid, etc. None of the approximately 30 pure compounds that were tested are new to us, i.e., they have also been tested by the Bureau of Entomology and Plant Quarantine, U. S. Dept. of Agriculture who also tested the addition of  $\text{CaCl}_2$  to repellent mixtures and found it of small value. Dr. Dörr emphasized that the addition of  $\text{CaCl}_2$  has a definite effect in extending repellency although Dr. Mudrow's testing data were somewhat meager to support his assertion. Dr. Dörr, when questioned about the  $\text{MgCl}_2$  in the "Mipax" formula, seemed to think that it was not particularly necessary but that someone thought it had an astringent effect on the skin. Without  $\text{CaCl}_2$  in the formula, "Mipax" or "Presinol" was found not very effective. With  $\text{CaCl}_2$  in the formula, the repellent gave 3 to 5 hours protection against Aedes aegypti in a cage test when the arm of the subject had been saturated with repellent applied with a sponge and the test started one hour after application.



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Illustrative of the effect of  $\text{CaCl}_2$  in a repellent mixture, the following data were obtained as the result of only a few tests:

10 g Cinnamyl alcohol  
90 g Ethanol (96%) 3 hours

10 g Cinnamyl alcohol  
90 g Ethanol (96%) 9 hours  
10 g  $\text{CaCl}_2$

### d. "Simplified Mipax"

A simplified "Mipax" recipe which is just as effective as the more elaborate one was given by Dr. Dörr as follows:

100 g Cinnamyl alcohol  
60 g Calcium chloride  
900 g Ethanol (96%)  
100 g Water

### e. Esters of Phthalic Acid.

Dr. Mudrow, who conducted the repellent tests found that diethyl phthalate as well as dimethyl phthalate as alcoholic solutions protected against Aedes aegypti for approximately the same length of time, i.e., about 2 to 3 hours. Dibutyl phthalate was found to give no protection.

### f. Repellent 50/181.

Trichloroacetylchlorethylamide,  $\text{Cl}_3\text{CCONHCH}_2\text{CH}_2\text{Cl}$ , was made at Leverkusen by Dr. Schweitzer. Dr. Mudrow at Elberfeld used a 7.5% alcoholic solution of this compound, and in a few tests it protected for about 7 hours. Dr. Mudrow stated that, at the concentration used, it was not at all irritating to the skin.

### g. Impregnation of Cloth with Repellents.

Rayon sleeves were impregnated with various repellents in alcoholic solution. The longest protection time obtained was about two weeks, which is considerably inferior to results obtained in the U.S.A.



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2. Comment on Repellent Testing At Elberfeld.

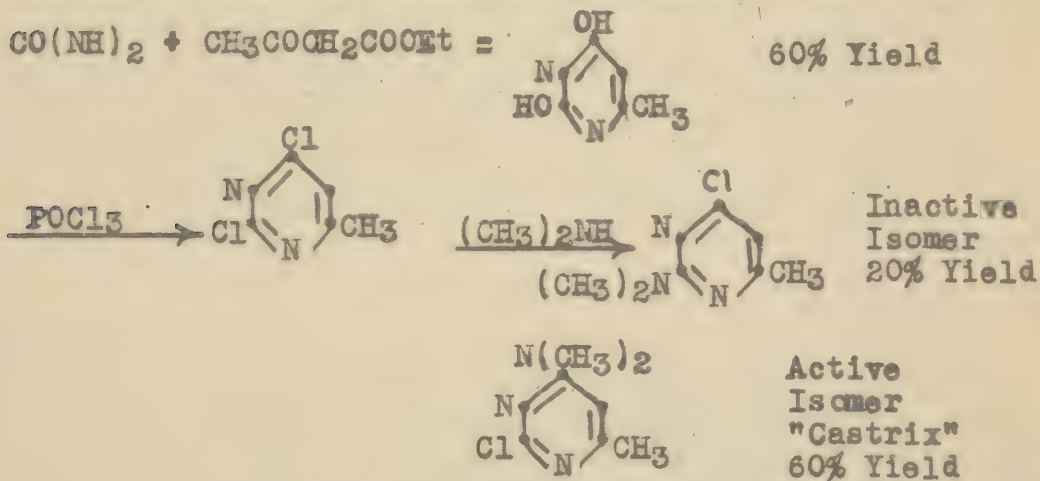
The repellent values obtained must be rather drastically discounted because the small cages housing the mosquitoes were not designed to allow sufficient ventilation, especially when volatile and odorous substances were used on the arm. No attempt was made to ascertain the biting-rate of the mosquitoes at any time on the untreated arm. Moreover, insufficient mosquitoes and test subjects were used. (See Appendix 3).

IV. RODENTICIDES

1. "Castrix"

a. At Elberfeld

"Castrix" or 2-chloro-4-methyl-6-dimethylaminopyrimidine, is a rodenticide claimed by Dr. Schönhöfer to be approximately 1/4 as toxic to rats as Strychnine. Dr. Westphal prepared it as follows:



2.  $p\text{-(CH}_3)_2\text{N-C}_6\text{H}_4\text{-N=N-SO}_3\text{Na}$

a. At Elberfeld.

This rodenticide, prepared by Dr. Schönhöfer



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is easily made by treating the diazonium salt from p-dimethylaminoaniline with  $\text{NaHSO}_3$ . This compound is not as toxic to rats as "Castrix" but it kills quickly and does not make the rats ferocious before death as does "Castrix". Either compound, according to Dr. Schönhöfer, when mixed with grain, is readily eaten by rats. "Castrix" has been used at 0.1% concentration in grain.

### 3. Comperison of 2 Rodenticides.

#### a. At Leverkusen.

Dr. Bonrath found "Castrix" more effective against mice; it is not quite as toxic against rats. The main objection to "Castrix" is its toxicity to higher animals. However, it has been found non-toxic to chickens, and other fowl at the concentration used. Grain is impregnated with 0.1% in water solution. The diazo compound is used at a higher concentration, namely, 0.6% and is better against rats. It is also toxic to larger animals and has not been tested against fowl.

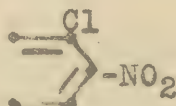
No attempts were made to determine the LD/50 of either compound. Dr. Bonrath stated, however, that approximately 60 mg/kilo of the diazo compound was lethal for mice, rats and cats. For "Castrix" he reckoned that approximately 6 mg/kilo was the lethal dose.

## V. FUNGICIDES

### L. P 1238

#### a. At Elberfeld.

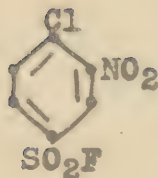
Dr. Pöhls made a series of compounds all containing the structure:



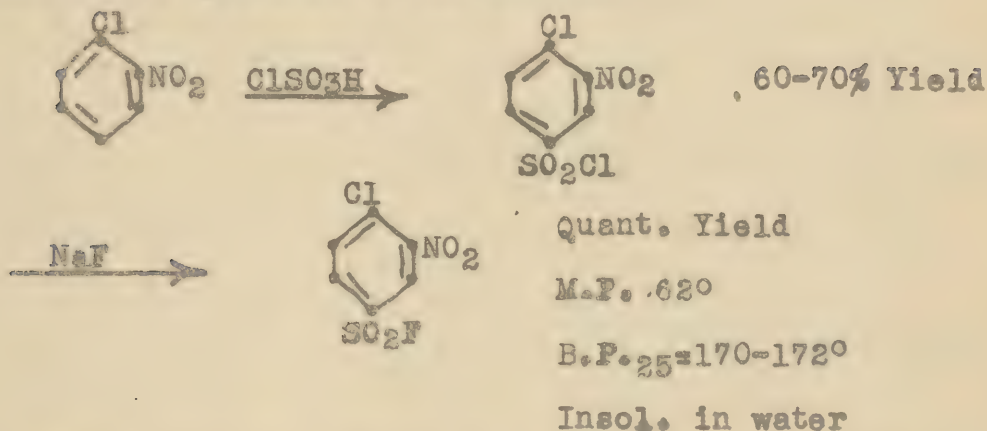
This structure, he claims, is essential to fungicidal activity. The meta and para position isomers were found inactive. The best compound of about 20 in this series is:



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Dr. Pöhl prepared it as follows:



The compound was tested in the laboratory against Penicillium, Coniphora and Fusicledium. In field tests it did not work as well. Although the compound can cause skin irritation it is described as otherwise harmless to humans and it causes no foliage injury.

2. 3-chloro-4-hydroxyphenyl-diazosulfonic acid, Sodium Salt.

a. At Leverkusen.

This compound was made by Dr. Urbschat and tested by Dr. Bonrath. Against a fungus disease of oats (Flugbrand) and against Fusarium nivale on rye, it has been found completely effective as a seed disinfectant. The seeds are soaked in a 0.1% water solution of the compound for 30 minutes.



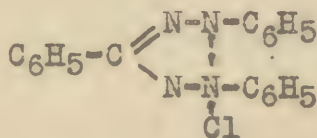
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VI. A COMPOUND FOR TESTING THE GERMINATION OF SEEDS.

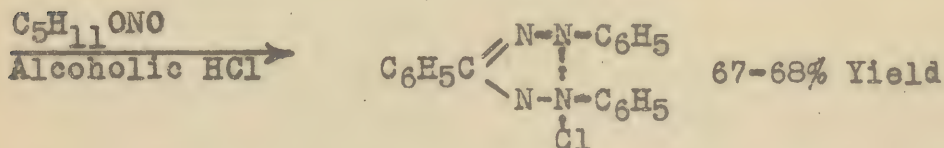
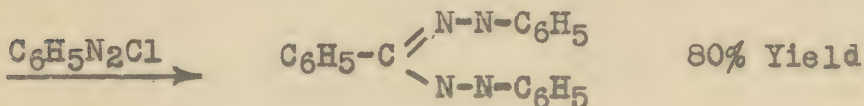
1. "Tetrazolium Salt"

a. At Elberfeld.

"Tetrazolium Salt"



or triphenyltetrazolium chloride is a compound prepared by Dr. Leuchs as follows:



The compound is colorless. Seeds that will germinate are colored red. (See Appendix 4).

b. At Leverkusen.

The compound is used as a 1 to 2% water solution. Cereal seeds (wheat, oats, corn, rye, barley, etc.) are soaked in the solution for 6 to 8 hours except in the case of oats which require 24 hours. The embryos of the seeds that will germinate turn red. Its chief advantage over the use of sodium selenide reagent in a germination assay is the non-toxicity of the tetrazolium salt.

## A P P E N D I X 1

### Preparation of 1,1-Di-chlorphenyl-2,2-dichloräthan

#### I. Chlorierung des Äthylalkohols.

In 1000 ccm denat. Alkohol wird unter anfänglicher Kühlung mit Leitungswasser Chlor eingeleitet derart, dass die Temperatur nicht höher als 30° ansteigt; beste Reaktionstemperatur: 25-30°. Die zunächst klare Lösung trennt sich allmählich in zwei Schichten; es entsteht eine untere Schicht, die allmählich an Volumen zunimmt auf Kosten der zunächst grossen oberen Schicht. Man leitet so lange Chlor ein, bis die obere Schicht nicht weiter abnimmt, was nach 4 1/2-tägigem Einleiten von insgesamt 3360 g Chlor eintritt. Die untere Schicht, die im wesentlichen aus einem Gemisch von Trichloräther, Dichloracetal und wenig Dichloracetaldehydhydrat besteht (vergl. A. 279,294), wird alsdann abgetrennt und ohne weitere Nachbehandlung direkt zur Kondensation eingesetzt; die obere Schicht besteht im wesentlichen aus wässriger Salzsäure. Man erhält:

untere Schicht: 985 ccm; d = 1,330; mithin = 1310 g

obere Schicht : 250 ccm; d = 1,255.

Bei zwei in gleicher Weise mit je 5 Ltr. Alkohol durchgeführten Versuchen wurden folgende Ergebnisse erhalten:

	untere Schicht	d	:	obere Schicht	d
a)	4500 ccm	1,330	:	1550 ccm	1,210
b)	5040 ccm	1,335	:	1375 ccm	1,252

#### II. Kondensation.

Zu 200 ccm conc. Schwefelsäure wird unter Kühlung bei einer Temperatur von 0 bis 5° ein Gemisch von 200 gr. Chlorbenzol und 160 gr. chlorierter Alkohol (d=1,315; bei 30° chloriert) allmählich zugetropft unter stetem kräftigem Rühren. Danach werden bei der gleichen Temperatur allmählich 200 ccm Oleum (d=1,900 bis 1,915) tropfenweise eingetragen. Danach wird ohne die Kühlung zu erneuern weitergerührt, sodass die Mischung sich allmählich wieder auf Zimmertemperatur erwärmt. Es wird mindestens 12 Stunden nachgerührt. Danach trägt man den ganzen Ansatz auf Eis aus, dekantiert die wässrige Schwefelsäure von dem krümelig abgeschiedenen Reaktionsprodukt und wäscht dieses alsdann säurefrei durch 5 bis 6 maliges Dekantieren mit Wasser. Nach der Neutralisation der letzten Schwefelsäurereste mit Natriumacetat wird zur Entfernung nicht



umgesetzten Chlorbenzols eine Stunde mit Wasserdampf destilliert, eventuell erneut aufgetretene Mineralsäure noch heiss mit Natriumacetat neutralisiert und alsdann unter kräftigem Rühren erkalten gelassen. Das zu kleinen kugeligen Aggregaten erstarrte Produkt wird alsdann abgesaugt mit etwas Wasser gewaschen und an der Luft getrocknet.

Ausbeute: 240 bis 245 gr.

Analyse: p-Verbindung 79,0%

m-Verbindung 17,3%

-----

mithin wirks. Subst. 96,3%

Paradichloraldehyd: 0,7%

Wasser : 3,0%

I. G. FARBENINDUSTRIE AKTIENGESellschaft  
SCHAFT Werk Elberfeld

## A P P E N D I X 2

### Substances Tested against Body Lice: Dr. Stötter






In den Tabellen sind die Eigenschaften von verschiedenen Präparaten, die sich gegen Kleiderläuse als besonders wirksam erwiesen haben, in Bezug auf Wirkung und bei den besten in Frage kommenden Typen auf Dauer der Wirkung dargestellt.

Was in den Tabellen für Pudermwirkung gezeigt wird, gilt in gleicher Weise bei Prüfung der Wirkstoffe angewandt in organischen Lösungsmitteln nach Art der chemischen Wäsche und auch bei Anwendung der Wirkstoffe aus Wasser, sei es als Emulsion oder als Dispersion.

In jeder der Anwendungsweise ergab sich die Überlegenheit des Chlorphenylchlormethylaulfon gegenüber den Vergleichsprodukten unter gleichen Versuchsbedingungen.

### 3 Beilagen

Die Bewertung in den Tabellen ist:

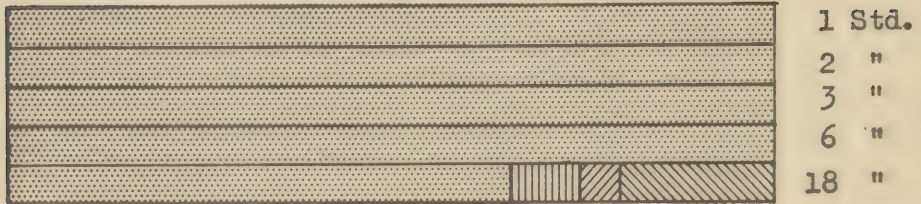
schwarz	=	Versuchstiere	ungeschädigt	=	
blau	=	"	leicht krank	=	
grün	=	"	krank	=	
gelb	=	"	schwerkrank	=	
rot	=	"	tot	=	



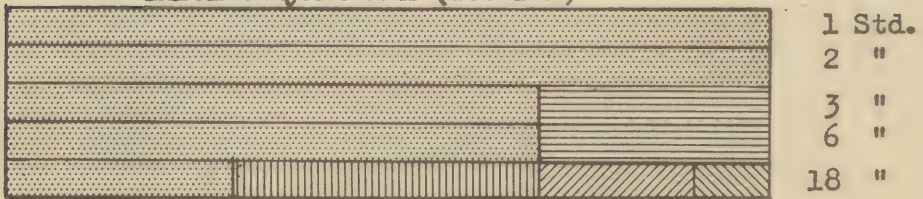
## Puderversuche gegen Kleiderläuse

Prüfungsergebnis bei Einwirkungsdauer von:

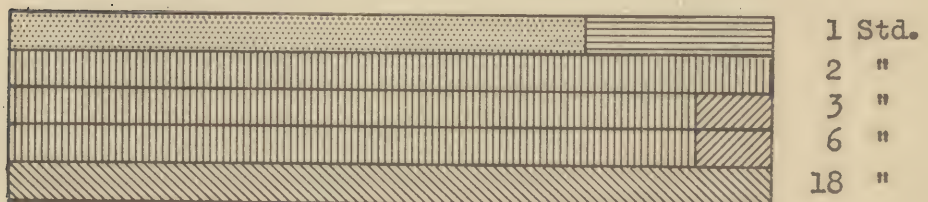
Blindversuch: Talkum - Kreide /2:1



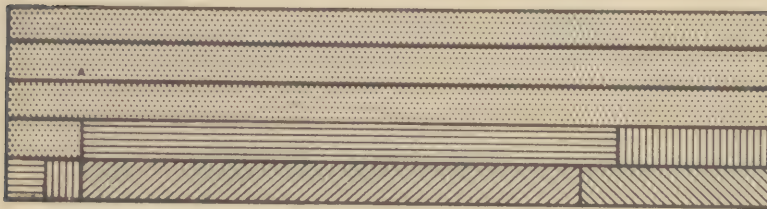
1%iger Puder von 4,4' Dichlordiphenyltri-  
chlormethylmethan (Gesarol)



1%iger Puder von 4 Chlorphenyltrichlor-  
methyl-Carbinol

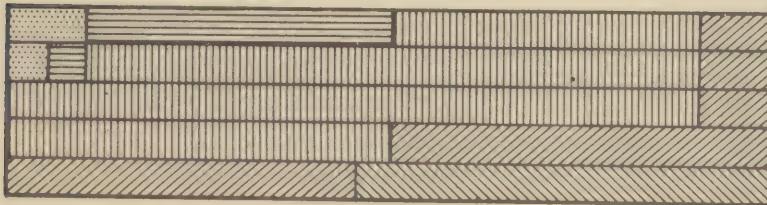


1%iger Puder von Pentachloräthylbenzol  
(Lucex)



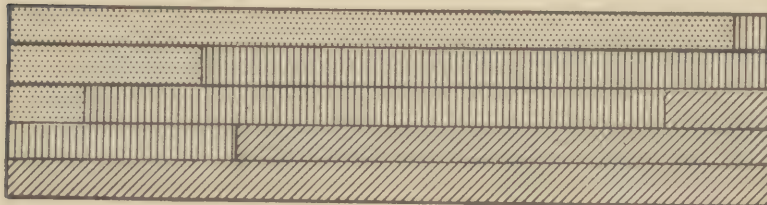
1 Std.  
2 "  
3 "  
6 "  
18 "

1%iger Puder von Butyroanisol



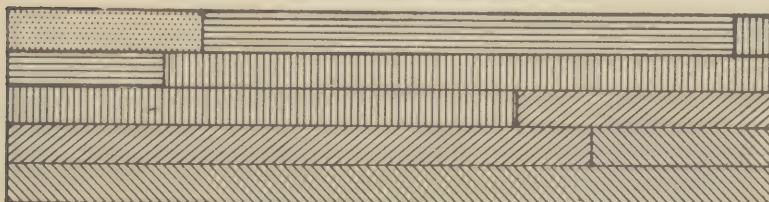
1 Std.  
2 "  
3 "  
6 "  
18 "

1%iger Puder von Trichloracetylchloräthyl-  
amid (50/181)



1 Std.  
2 "  
3 "  
6 "  
18 "

0.3%iger Puder von 4-Chlorphenylchlor-  
methylsulfon (Lauseto-neu)



1 Std.  
2 "  
3 "  
6 "  
18 "

Puderbasis: 2 Teile Talkum, 1 Teil Kreide.  
Versuchsanordnung: je 20 Versuchstiere in  
Petrischalen auf Stoffproben, auf die  
gleiche Mengen Puder dünn aufgetragen  
waren.

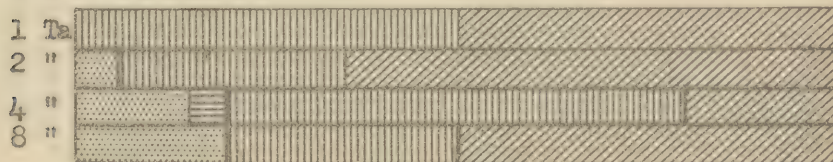


Prüfung gegen Kleiderläuse.  
(Belüftungsversuch)

Die eingepuderten Proben wurden vor der Prüfung gegen Kleiderläuse einen, zwei, vier und acht Tage belüftet und dann im üblichen 18 Std.-Versuch geprüft.

1%iger Puder aus 4,4' Dichlordi-  
 phenyltrichlormethylmethan

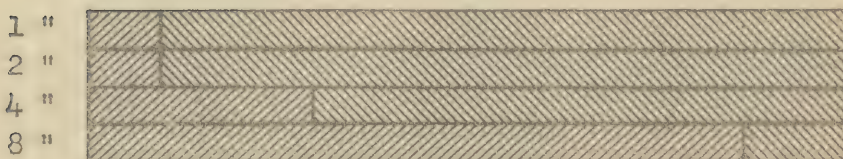
belüftet:



1%iger Puder aus Pentachloräthyl-  
 benzol



1%iger Puder aus 4-Chlorphenyl-  
 chlormethylsulfon.



Die Versuche wurden wie stets unter ganz gleichen Bedingungen mit gewichtsmäßig gleichen Pudermengen ausgeführt.

## Prüfung gegen Kleiderläuse.

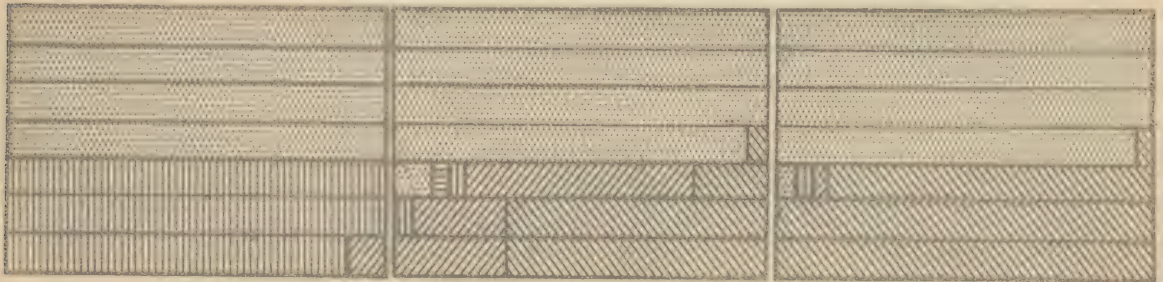
Vergleich von Pentachloräthylbenzol, 4,4<sup>e</sup> Dichlordiphenyltrichlormethylmethan und 4-Chlorphenylchlormethylsulfon bei zeitlich beschränkter Einwirkungsdauer.

### I. 4%iger Puder von Pentachloräthylbenzol

Zustand der Larven:

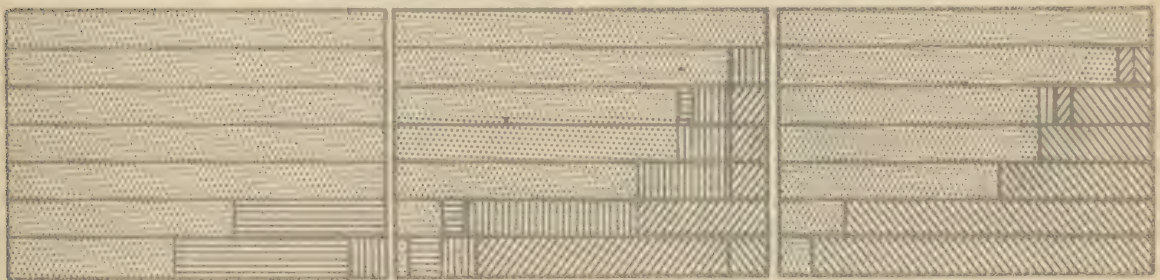
direkt nach Puderberührung. nach 24 Stdn.

nach 48 Std.



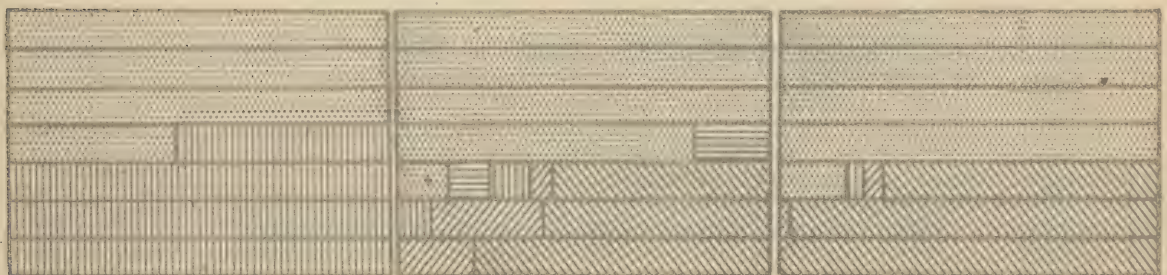
Puderberührung: (top to bottom) 1, 4, 30 Minuten;  
1, 3, 4, 6 Stunden.

### II. 4%iger Puder von 4,4<sup>e</sup> Dichlordiphenyltrichlormethylmethan



Puderberührung: (top to bottom) 1, 4, 30 Minuten;  
1, 3, 4, 6 Stunden.

### III. 1%iger Puder von 4-Chlorphenylchlormethylsulfon



Puderberührung: (top to bottom) 1, 4, 30 Minuten;  
1, 3, 4, 6 Stunden.

Die Versuchstiere wurden 1 - 4 - 30 Minuten, 1 - 3 - 4 - 6 Stunden auf eingepuderten Stoffproben gehalten und dann abgenommen und ihr Zustand sofort, nach 24 Stunden und nach 48 Stunden beobachtet.



### A P P E N D I X 3

#### Insecticides and Repellents Produced and Tested by I. G. Farbenindustrie, Leverkusen.

Note: It should be noted that the "Pb" numbers represent the number assigned to a test specimen and not necessarily a new and different substance. New substances are designated by other letters and/or numbers. This should be borne in mind when reading the correspondence.

H. Hörlein

#### I. Lists of Preparations Tested

A. Anti-mosquito preparations from Leverkusen, related to Gesarol, that were tested in Wuppertal-Elberfeld.

Pb 460 = Lauseto (Gesarol) was effective for 12 months in the contact experiment (2); after that time, testing was discontinued.

Pb 461

462

463

See correspondence of 17 Feb. and 3 April 1944.

464

465

Formulas in part in later correspondence

466

Pb 544

545

See correspondence of 24 April and 19 May 1944

546

Pb 637

638

639

640

641

642

643

See correspondence of 15 June, 26 July, 10 Aug.

644

1944

645

646

647

Formulas in Section II

648

649

650

651

652

#### B. Other Mosquito-preparations

Pb 756

757

Pb 758  
759 See correspondence of 24 Aug. and 23 Oct. 1944  
760  
761 Formulas also to be found there  
762  
763  
764  
Pb 805  
806  
807  
808  
809 See correspondence of 5 Sept. 1944 and 10 Jan. 1945  
810  
811 Formulas also to be found there  
812  
813  
814  
815  
816

## II. Testing Methods, Correspondence, and Reports of Tests

### A. Testing of the Anti-Mosquito Preparations

1. Repellent effect. Designation of experiment MU.
  - a. On bare skin (arm).
  - b. On cloth drawn over the arm (stocking-type knitting).

2. Mosquitocide effect (contact effect, corresponding to that of Gesarol). Designation of experiment Ge.

a. The uncovered arm of the experimental persons is rubbed with the liquid (i.e. dissolved in a solvent) preparation; after one hour the first test is made in the mosquito cage. If an effect is found, the tests are continued hourly, 7 - 8 hrs. in all. The substance used for comparison is Mipax (Presinol) which has a standard effect of 3 - 5 hrs. The mosquitoes are in gauze-covered wire cages of a base of approx. 30 x 40 cm and a height of 30 cm. A full cage contains about 300 mosquitoes (males and females in about equal proportions). The preparation is considered as having effect if within a 5 min. period of exposure no mosquito bites. If, up to 4 mosquitoes bite within the 5 min. period, this is considered a trace effect; if more than 5 mosquitoes bite within 5 minutes or even a shorter period, the preparation is designated as ineffective. The "landing" of the mosquitoes without biting is not counted in the evaluation.

b. The cloth test is performed in the same manner. In certain instances the effect was examined also immediately after the saturation of the cloth with the preparation.



c. In the test for mosquitocide effect of the Gesarol type, 10 mosquitoes are placed in cages whose muslin walls have been saturated with the substance in question. An hourly record is kept of the behavior of the mosquitoes. The cages consist of a cube shaped wire frame whose sides are 10 cm long; they are covered with removable muslin tubes. These muslin tubes are soaked with the substance to be tested which is dissolved in ether, acetone, or a similar solvent, and then they are dried in air. The first test takes place the following morning, about 16 hours after the muslin tubes were treated. If the preparation possesses a mosquitocide effect, it is examined again after 14 days, 1 month, and later, as long as the efficacy lasts. The cages are stored away in the meantime, without renewed treatment of the muslin.

Evaluation of the efficacy:

W = Wirkung (effect) (80-100% of the mosquitoes in the cages are dead).

Sp.W. = Spur Wirkung (Trace Effect) (40-70% of the mosquitoes in the cages are dead; the others may be injured).

g.Sp.W. = geringe Spur Wirkung (Slight Trace Effect) (20-30% of the mosquitoes are dead, while the others may display injuries).

## B. Correspondence and Reports of Tests

Chemotherapeutic Laboratory

TO: Dr. Wegler, Leverkusen, Wissenschaftliches Hauptlaboratorium (Principal Scientific Laboratory).

Prof. Md./F. 10 Jan. 1945

Anti-mosquito substances.

Since our investigation of the substances which you sent with a letter of 5 Sept. 1944 for testing in regard to their anti-mosquito effect, have reached a certain finishing point, and since at present due to the lack of insect material we are able to perform only a limited number of tests, I should like to present to you the results obtained until now. This is most simply accomplished by means of a tabulated survey chart, from which you are able to read off the efficacy or lack thereof of the individual compounds with the various testing methods. The preparations which you numbered 1 - 12 received with us, in continuous numbering, the designations PB 805-816.

In the tests for the mosquito repellent quality the undiluted solutions were used; in testing in contact experiments, on the other hand, the substances were diluted

for reasons of economy to their three-fold amount by means of acetone; the mosquito cages were thus impregnated with a 2½% solution. After drying, the mosquitoes were placed in the cages only 16 hrs. later, and the effect was then tested hourly for 8 or 9 hrs. If the limit of the efficacy of a substance is not reached by this point, the investigations of the contact effect are then continued even beyond this point.

The long duration of the tests is explained in part by the necessity of repetitions when the results were not clear, and in part also by a high mortality rate in the mosquito cages after tests for the repellent effect. Those mosquitoes which did not bite, but which at times flew against the arm of the experimental persons, also come into contact with the preparation and die because of the contact effect, so that the mosquitoes in the test cages had to be replenished much more frequently from our none-too-extensive mosquito cultures than in the case of preparations without this effect.

Since Director Dr. Schönhöfer of the Scientific-Chemical Laboratory here is also participating in the testing of anti-mosquito substances, I should like to ask you to send him also copies of your letters.

Chemotherapeutic Laboratory  
/s/ Dr. Mudrow



I.G. Wuppertal-Elberfeld  
Chemo.-Labor.

Table I: Tests performed on the arms of experimental persons in regard to mosquito repellent effect.

After ... hours	Pb 805	Pb 806	Pb 807	Pb 808	Pb 809	Pb 810	Pb 811	Pb 812	Pb 813	Pb 814	Pb 815
1	Sp	Ø	Ø	W	W	W	W	W	W	W	W
2	W	W	SpSp	Sp	Sp	Sp	Sp	Sp	Sp	Sp	Sp
3	Sp	W	Ø	Ø	Ø	Ø	Ø	Ø	Ø	Ø	Ø
4	Ø	Ø	Ø	Ø	Ø	Ø	Ø	Ø	Ø	Ø	Ø
5	Ø	Ø	Ø	Ø	Ø	Ø	Ø	Ø	Ø	Ø	Ø
6	Ø	Ø	Ø	Ø	Ø	Ø	Ø	Ø	Ø	Ø	Ø
7	Ø	Ø	Ø	Ø	Ø	Ø	Ø	Ø	Ø	Ø	Ø

W = Wirkung (Effect): no mosquito bites within 5 min.

Sp = Spurwirkung (Trace effect): up to 4 mosquitoes bite within 5 min.

Ø = No effect: more than 5 mosquitoes bite within 5 min. or less.

I. G. Wuppertal-Elberfeld  
Chemo.-Labor.

To the Coloristic Dept., Attn: Dr. Drapel, Leverkusen.

Dr.Dr./G. 29 Sept. 44 Dr.Md./B. 20 Sept. 1944

Anti-mosquito substance Schweitzer 50/181.

Preparation Schweitzer 50/181, heated in a reflux condenser, was examined several times by means of the mosquito tests, in which with various experimental persons it displayed a period of efficacy of 3 to 7 hours. Thus in comparison to the fresh preparation it showed no decrease of effect, since in biological tests one must always calculate with certain fluctuations.

The testing of the 9 solutions which you sent with your letter of 24 Aug. has been possible only on 9 days, and I should like to repeat the tests before sending you my findings.

Chemotherapeutic Laboratory

/s/ Dr. Mudrow

\* \* \* \*

I. G. Leverkusen  
Principal Scientific Lab.

To: Dr. Mudrow

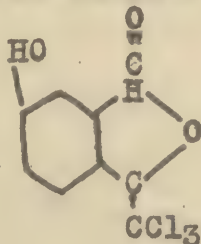
I. G. Werk W.-Elberfeld Dr. Wg/Oe. 5 Sept. 1944

Re: I am glad to accept your kind offer, made recently via long-distance telephone call, of examining some further substances for their effect against mosquitoes, and I am sending you a number of compounds for testing. The majority of these compounds belongs to the Benzyl alcohol series, of which you have already examined 3,4-dichlorbenzyl alcohol which you found quite effective.

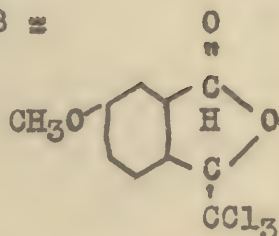
1. (Pb 805) benzyl alcohol (omit this if you have already tested it),
2. (Pb 806) 4-methoxybenzyl alcohol,
3. (Pb 807) 4-isopropylbenzyl alcohol (smelling substance),
4. (Pb 808) F 97 = dimethylbenzyl alcohol,
5. (Pb 809) F 141 = ethylbenzyl alcohol,
6. (Pb 810) F 163 = menaphtyl alcohol,



7. (Pb 811) phenozyethanol,  
 8. (Pb 812) F 146 = benzylacetoacetic ester,  
 9. (Pb 813) F 160 = di(p-chlorbenzyl)-acetoacetic ester,  
 10. (Pb 814) F 163 = 3.4-dichlorbenzylacetoacetic ester,  
 11. (Pb 815) F 167 =



12. (Pb 816) F 168 =



all products are 7½% solutions in acetone or methanol.

Wegler.

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I. G. Wuppertal-Elberfeld  
 Chemo.-Labor.

Coloristic Department, attn, Dr. Drapal, Leverkusen.

Dr.Dra./P. 24.Aug.1944 Letter No. 8488 Dr.Md./B 23 Oct.1944

Test for mosquito-repellent effect;

As the result of difficulties in the breeding of mosquitoes it was not possible for me to undertake the intended 2nd repetition test of all preparations you sent us in August. So that you will have to wait no longer, I wish to send you today the results obtained on the various days of the first tests. The solutions were applied to the arms of the experimental persons. In the 2nd mosquito experiment the test of the 5th hour had to be omitted because of air-raid alarm.

Pb 765-M/29	1.) 5hW.6hSp.W.7hø	Pb 761-M/34	1.) 1hW.2hSp.
	2.) 3hW.4-8h Sp.W.		W.3-6hW.7hSp.W
			2.) 6hW.7hø
Pb 757-M/30	1.) 3hW.4hø	Pb 762-M/35	1.) 1hø
	2.) 4hW.6hø		2.) 1hSp.W.2hø
Pb 758-M/31	1.) 3hW.4hø		3.) 1hø
	2.) 3hW.4hø	Pb 763-M/36	1.) 1hø

Pb 759-M/32 1.) 2<sup>hw</sup>.3<sup>h</sup>Sp.W.4<sup>h</sup>Ø  
2.) 3<sup>hw</sup>.4<sup>h</sup>Sp.W.6<sup>h</sup>Ø

2.) 1<sup>h</sup>Sp.W.2-3<sup>h</sup>  
W.4<sup>h</sup>Sp.W.6<sup>h</sup>Ø

Pb 760-M/33 1.) 4<sup>hw</sup>.5<sup>h</sup>Ø  
2.) 4<sup>hw</sup>.6<sup>h</sup>Sp.W.7<sup>h</sup>Ø

Pb 764-M/37

3.) 1<sup>h</sup>Ø  
1.) 2<sup>hw</sup>.3<sup>h</sup>Sp.  
W.4<sup>h</sup>Ø  
2.) 6<sup>hw</sup>.7<sup>h</sup>Sp.W.

The findings show that preparations Pb 762 and 763 are unequivocally the poorest; however, in regard to the better effect it is more difficult to make gradations. Nevertheless it appears that none of the preparations is effective enough to warrant testing in a higher dilution.

The above-mentioned difficulties in our mosquito-breeding were largely caused by the testing of these preparations. The repellent effect frequently becomes apparent in the fact that the mosquitoes fly against the arm of the test person but do not bite. In flying against the arm they come into contact with the preparation and sooner or later they come victim to its killing effect. In any case, after such a mosquito test we always observed an especially high mortality rate in our mosquito cages. In order to convince ourselves of the mosquitocide effect of the substance tested, another test was conducted on the order of a Gesarol test (insertion of 10 mosquitoes into cages impregnated with the substance; hourly observations of the effect). In order to save substance, the solutions were diluted to one-third by means of alcohol, resp. acetone, i.e. were tested as 2 $\frac{1}{2}$ % solutions. The results were the following:

Pb 756 after 1<sup>hw</sup>. (all mosquitoes dead) Pb 757: 1<sup>hw</sup>., Pb 758: 1<sup>hw</sup>., Pb 759: 1<sup>hw</sup>., Pb 760: 1<sup>hw</sup>., Pb 762: 3<sup>hw</sup>., Pb 763: 3<sup>hw</sup>., Pb 764: 1<sup>hw</sup>.

From these results you will observe that the contact effect of these substances, as we already know it, is so strong that it interferes with the tests of the repellent effect of the substances, especially since we do not have unlimited numbers of mosquitoes at our disposal. I should like to ask you therefore, to have patience until I am able to send you the results of the further testing.

Chemotherapeutic Laboratory  
Elberfeld

/s/ Dr. Mudrow.



I. G. Wuppertal-Elberfeld  
Chemo.-Labor.

Table 2: Test for toxic contact effect.

Effect after:	Pb 805	806	807	808	809	810	811	812	813	814	815	816
16 hrs.	7 <sup>h</sup> g.Sp.	3bw	1bw	1bw	2bw	4bw	6bw	6bw	6bw	5bw	8bw	8h
14 days	9 Sp.	8bw	8bw	9bw	2bw	8bw	6bw	8bw	8bw	8bw		
1 month				8bw	6bw	8bw	7bw		:	:		
1½ months					:	8bw.Sp.	:		8bw.Sp.	8bw		
2 months					7bw	8bw.Sp.	7bw					
3 months					8bw	8bw.Sp.	8bw.Sp.					

W = Wirkung (Effect): 80 - 100% of the mosquitoes died.

Sp = Spur Wirkung (Trace Effect): 40 - 70% of the mosquitoes died.

g.Sp. = geringe Spur Wirkung (Slight trace Effect): 20 - 30% of the mosquitoes died.

I. G. Leverkusen

Coloristic Department

TO: Chemotherapeutic Laboratory      Ø Dir.Dr.Schönhöfer  
" Prof.Dr.Bayer

Dr.Dra/G

29 Aug. 1944

Anti-mosquito substance Schweitzer 50/181.

To determine the storage ability of the anti-mosquito substance, dissolved in alcohol, we have heated the inclosed substance for several days in a reflux condenser and we request you to examine this solution in comparison with the fresh solution of Schweitzer 50/181, recently sent to you, for their anti-mosquito action.

sent:  
1 sample

Eulan tech.  
/s/ Drapal

\* \* \* \* \*

I. G. Leverkusen  
Coloristic Department

Eulan Technisch

Confidential

Via: Director's Section      Ø Dir.Dr. Schönhöfer  
TO: Chemotherapeutic Labor., Elberfeld " Prof.Dr.Bayer

Dr.Dra/P.

24 Aug. 1944

Test for mosquito-repellent effect.

In the quest for mosquito-repellent substances of lasting effect and of a certain distance effect we have prepared a series of preparations which we hope will have the sought-for effects.

We ask you therefore to test the 9 100cc samples of solutions, sent to you under separate cover, according to these points of view by direct rubbing upon the skin, and to determine the most suitable product by investigating degrees of dilution.

All of these solutions contain 7.5% active ingredients and, with exception of M/36 which is dissolved in acetone, they are alcoholic (denatured) solutions. Designations of the products, whose compositions are sent to you separately, are as follows:



1. (Pb 756) M/29: Schweitzer 50/181 (for comparison)
2. (Pb 757) M/30: Schweitzer 50/181 + Meiser 1700 (1:1)
3. (Pb 758) M/31: Schweitzer 50/181 + Muth 2567 (1:1)
4. (Pb 759) M/32: Lober F/95 + Meiser 1700 (1:1)
5. (Pb 760) M/33: Lober F/95 + Muth 2567 (1:1)
6. (Pb 761) M/34: Lober F/169
7. (Pb 762) M/35: Meiser 1700
8. (Pb 763) M/36: Wegler 24844
9. (Pb 764) M/37: Schweitzer 50/181 + 15% Tylose TWA 25.

It is requested that the 5 substances, M/29, M/30, M/31, M/33, and M/37 be given preferred treatment, if possible.

Incl: 1 list of compositions                      Eulan techn.  
       9 Solutions (separate)                    /s/ Drapal

Incl:


Compositions of the products named in the letter.

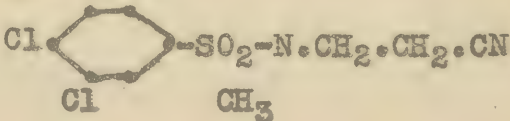
Schweitzer 50/181:  $C_6Cl_3.CO.NH-C_2H_4Cl$ .

Meiser 1700:  $CHCl_2.CH \begin{cases} C_6H_4Cl \\ C_6H_4Cl \end{cases}$

Muth: 2567:  $C_6H_5.SO_2.CH_2.Cl$

Lober F/95: 2,6 . dichlorbenzyl alcohol

Lober F/169: 

Wegler 24844: 

\* \* \* \* \*

I. G. W.-Elberfeld  
 Chemo.-Labor.

TO: Coloristic Dept.,  
 Leverkusen, attn: Dr. Drapal Dr.Md./Felg. 10 Aug.1944

Mosquito repellents.

According to our agreement via telephone with Dr. Wegler, of 31 July, we have tested 4 of your mosquito repellents as to their mosquitocide effect. The mosquito cages

were impregnated with the 7.5% alcoholic solutions; as in other experiments, the mosquitoes were inserted in the cages 16 hrs. later. The result was the following:

Pb 643 after 1 hr., effect.  
Pb 644 after 2 hrs., effect.  
Pb 745 after 4 hrs., effect.  
Pb 649 after 2 hrs., effect.

Chemotherapeutic Laboratory

/s/ Dr. Mudrow

\* \* \* \* \*

- I.G. W.-Elberfeld -  
ChemoLabor.

TO: Coloristic Dept., Leverkusen, attn: Dr. Drapal.

Dr.Dra/P 15 June, 19 June, 10 July. Dr.Md./Felg. 26 July 44

Test for mosquito-repellent effect.

In extensive experimental series we have examined the 16 substances, sent to us in June, for their mosquito-repellent effect, and in comparison with Mipax we have obtained the results shown in the inclosed tables. The preparations were tested in the order shown in your letter; they were given the numbers Pb 637 - 652. According to the results of the tests, the most effective substances were Pb 637 = Schweitzer 50/181, which also in the test on the bare skin in its original concentration remained effective for 7 hrs., and Pb 644 - Lober V/752 whose effect was somewhat poorer when tested upon the arm (1 - 3 hrs., trace effect; 5 hrs., without effect). The group Pb 640, 641, 642, 646-650 was almost equally effective in the form of a 7.5% solution, but differences became evident in the 10-fold dilution. Also Pb 638, 639, 643 had relatively good effect, whereas Pb 645, 651, and 652 had considerably poorer results so that tests for these substances were discontinued.

With the values obtained it must be stressed that, with the exception of a preliminary test, we are dealing in each case with the results of only one mosquito test, since more detailed investigations could not be performed for reasons of time, personnel, and material (limited number of mosquitoes). Thus it may be that in individual cases certain shifts of value occur (e.g. between effect and trace



effect, or between trace effect and no effect, as is always the case in biological tests) or that differences appear between the individual experimental persons. But on the whole it is assumed that the results give a correct picture.

The 5% solution of Schweitzer 50/181 = Pb 544 has not yet undergone testing, but in agreement with your wishes we have undertaken a rinsing test on the arm and are thus able to confirm your observations. After the arm was rinsed with water even for several minutes and then permitted to dry in the open air, the effect was retained; to be sure it disappeared when warm water was used or when the arm was rubbed energetically with a towel.

Chemotherapeutic Laboratory

/s/ Dr. Mudrow

Table 1. Mosquito repellents from Leverkusen 7.5% methanol solution.

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Sub-	637	638	639	640	641	642	643	644	645	646	647	648	649	650	651	652	Mipax
stance																	
immed.	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W
1 hr.	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W
3 hrs.	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W
5 hrs.	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W
7 hrs.	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W
24 hrs.	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W
72 hrs.	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W
14 days	SpW	SpW	SpW	SpW	SpW	SpW	SpW	SpW	SpW	SpW	SpW	SpW	SpW	SpW	SpW	SpW	SpW

W. = no mosquito bite in the course of 5 min.  
 Sp.W. = up to 4 mosquitoes bit in the course of 5 min.  
 Ø = 5 or more mosquitoes bit in the course of 5 min.

Table 2. Mosquito repellents from Leverkusen 0.75% methanol solution.

Nr.	1	2	3	4	5	6	7	8	10	11	12	13	14	17
Sub-	637	638	639	640	641	642	643	644	646	647	648	649	650	Mipax
stance														
immed.	W	W	W	W	W	W	W	W	Ø	W	W	W	W	W
1 hr.	W	W	W	W	W	W	W	W	Ø	W	W	W	W	W
3 hrs.	W	W	W	W	W	W	W	W	Ø	W	W	W	W	W
5 hrs.	W	W	W	W	W	W	W	W	Ø	W	W	W	W	W
7 hrs.	W	W	W	W	W	W	W	W	Ø	W	W	W	W	W
24 hrs.	W	W	W	W	W	W	W	W	Ø	W	W	W	W	W
72 hrs.	W	W	W	W	W	W	W	W	Ø	W	W	W	W	W



Coloristic Department

Chemotherapeutic Institute .

Ø Dir. Dr. Schönhöfer

W.-Elberfeld

Dr.Dra./P. 10 July 1944

Re: Mosquito Repellents.

In connection with our letter of 15 June 1944 we inform you that in a practical test with preparation M/12 (= Schweitzer 50/181) we observed a remarkable resistance against rinsing away of the mosquito-repellent effect upon the skin. Since this property may be of significance for bathers, for example (in an open sun bath), we should appreciate if you would check on our observation.

Eulan technic.

for Dr. Drapal

\* \* \* \* \*

I. G. Leverkusen

Coloristic Department

TO: Chemotherapeutic Laboratory Ø Dir. Dr. Schönhöfer

W.-Elberfeld

Dr.Dra./P

19 June 1944

Re: Test for mosquito-repellent effect.

In reference to our letter of 15 June 1944 we should like to ask you to include also the following products in the test series:

- 12. (648) M/4 = Schmelzer 196/33
- 13. (649) M/25 = Lober F/87
- 14. (650) M/26 = Schröter R/108
- 15. (651) M/27 = Retter 694
- 16. (652) M/28 = Schrader 11/61

The concentration is the same as in the 11 substances sent to you 15 June, i.e. 7.5% in alcohol.

Incl.:

Coloristic Department

5 preparations @ 50 cc.

-s- Dr. Christ

\* \* \* \* \*

I. G. Leverkusen

Coloristic Department

TO: Chemotherapeutic Laboratory    Ø Dir.Dr.Schönhöfer

W.-Elberfeld    Dr.Dra./P. 15 June 1944

Test for mosquito-repellent effect.

We thank you for the test findings on the preparations  
Schweitzer 50/181 (Pb 544) and  
Lober 3/340 b (Pb 546)

in which you judge very favorably on the mosquito-repellent effect of these two products. Since with this result we naturally are greatly interested in testing other substances of similar composition, we gladly make use of your willingness to perform further investigations for us. Thus we are sending you under separate cover 11 additional preparations, which, like Mipax, are 7.5% and were dissolved in alcohol. In each instance we send 50 cc of:

1.	(Pb 637)	Schweitzer	50/181	(Numerical sequence Le:M/12
2.	(Pb 638)	"	52/120a.	" " M/16
3.	(Pb 639)	"	52/121b	" " M/17
4.	(Pb 640)	"	53/52	" " M/18
5.	(Pb 641)	"	53/53	" " M/19
6.	(Pb 642)	"	53/4b	" " M/20
7.	(Pb 643)	Lober	F/95	" " M/21
8.	(Pb 644)	"	V/762	" " M/15
9.	(Pb 645)	"	748/2	" " M/22
10.	(Pb 646)	Schommer	1439	" " M/23
11.	(Pb 647)	Muth	2597/II	" " M/24

We request you to perform the tests again, to the extent as the quantities sent permit it, on the inclosed stocking-weave and also on the bare skin, and to determine in this both the intensity of the initial effect and also that of a permanent effect.

We also request you to compare the most effective products appearing from this test in an additional series of tests, comparing them with each other and with Mipax, by changing both concentrations and time, until it becomes unequivocally apparent which of the products is the most effective. In this it is recommended to include in the test series also substance P 544, as this received especially favorable mention in the first tests. A gradation in concentration, as might be required, may be undertaken by suitable dilution with alcohol.



To give the product with the greatest initial effect a greater permanent effect, we also request you to carry out a test in which this product is mixed with parts of that product which in itself has the greatest permanent effect.

Coloristic Department

/s/ Dr. Christ

\* \* \* \* \*

I.G. W.-Elberfeld  
Chemo.-Labor.

TO: Coloristic Department, Leverkusen, attn: Dr. Drapal

Dr.Dra./P. 24 April Dr.Md./Br. 19 May 1944

Test for mosquito-repellent effect.

The 5% alcoholic solutions sent to us at the end of the past month of 1.) Schweitzer 50/181 (= our No. Pb 544), 2.) Schweitzer 50/181 + V 762 (1:1) (= Pb 545), and 3.) V 762 (purified Lober 3/340 b) (= Pb 546) were sprayed upon the stocking-knit weaves Bemberg/Cotton and Silk/Cotton (sent with the solutions) and tested for their mosquito-repellent effect. First a preliminary experiment had been performed with a small number of mosquitoes in order that not too many mosquitoes would be lost by the mosquitocidal effect which is also present in the substances. Already this preliminary showed a certain mosquito-repellent effect immediately after spraying, and an hour later; after 5 hrs. isolated mosquitoes began to bite in the cases of Pb 545 and 546. The subsequent test with full mosquito cages (several hundreds of female mosquitoes) yielded the surprising result that at all times (Immediately, after 1, 3, 5, and 7 hrs.) occasionally, or with every sample, the mosquitoes flew against the arms of the experimental persons, covered with sprayed weaves, but that not one single bite took place. Their desire to bite, on the other hand, was shown by the fact that they settled upon the uncovered arms in large quantities, and bit, but only those areas of skin which had not been in contact with the treated material. This result induced me to test the various solutions also without cloth directly on the arm, on the order of Mipax. In this the mosquito-repellent effect was confirmed, which with Pb 544 lasted for 6 hrs. and with the two other substances for 4 hrs. each, as also in the case of Mipax which was tested simultaneously, for the sake of comparison. To be sure, the mosquitoes again flew against the arm (which happens more rarely in the case of Mipax, but they did not bite. It is now my intention to test the solutions once

more in connection with the cloth materials, in comparison with materials sprayed with Mipax; I shall inform you on this when the experiments are completed.

It is extremely disagreeable for me to have to inform you that the flacon which you sent for spraying arrived here in a damaged and useless condition. By whom and how this accident happened was no longer to be determined. I regret this especially since in present conditions we are not in the position to repair the damage. We shall at least attempt to have one of our fine mechanics repair at least the spraying mechanism.

For spraying the materials we used at first for the time being a flower spray. But since this method appeared too complicated and since in spraying from nearby the thin weaves were nevertheless soaked, we have in the main experiment, soaked the cloth completely with the solution in question, which always dried relatively rapidly, and this we also intend to do with Mipax.

As an addendum I should like to give you the result of the recent tests with the mosquitocide substances.

Pb 460 - Lauseto    Pb 461-Muth 2509/1    Pb 465-  
Piepenbrink  
3084

1 month	4 hrs., effect	6 hrs., effect	no effect
2 months	3 hrs., effect	8 hrs., trace effect	

Chemotherapeutic Laboratory

Dr. Schönhöfer  
Dr. Dörr

/s/ Dr. Mudrow

\* \* \* \* \*

I. G. Leverkusen  
Coloristic Department

TO: I.G. Wuppertal-Elberfeld

Chemotherapeutic Laboratory Dr.Dra./P. 24 April 1944

Dr.Md./B. 3 April 1944

Test for mosquito-repellent effect.

in your report of 3 April 1944 we are especially interested in the test results on the preparations:

Pb 463 = Schweitzer 50/181

- 41 -      Pb 466 = Lober 3/340 b,



as these substances, to be sure, do not display a lasting, but a very rapid effect and thus might possibly be used as spraying substances as, for example, on stockings. For determining such possibilities we sent you 200 cc of 5% alcoholic solutions of each of the following:

1. (Pb 544) Schweitzer 50/181
2. (Pb 545) Schweitzer 50/181 + V/762 (1:1)
3. (Pb 546) V/762 (= purified Lober 3/340 b), and also:
4. 6 m stocking weave Bemberg/Cotton
5. 6 m stocking weave Silk/Cotton
6. 1 30-cc-flacon for spraying.

To approximate the conditions of practice, we propose that the tests be performed in such a manner that in each case a type of stocking weave be drawn over the arms of suitable test persons and that immediately after the spraying of the individual preparations their mosquito-repellent effect be tested at once, after 1 hr., and after 5 hrs.,. If the spray should fail temporarily in the flacon, which may occur when air is pumped in, one unscrews the press button with the valve, shakes it out, and again screws it on.

If for the execution of the tests you should require additional quantities of the substances and of the knit materials we can furnish you with them. After completion of the tests we request you to return the spraying flacon to us, as it was borrowed from a private owner.

sent under separate cover:  
2 knit materials and chem.  
substances  
1 spraying flacon  
3 bottles

Eulan techn.  
/s/ Dr. Drapal

\* \* \* \*

I. G. Leverkusen  
Coloristic Department

TO: Chemotherapeutic Laboratory

Elberfeld

Dr.Dra./P.

17 Feb. 1944

Test for mosquito-repellent effect.

We request you to test the following preparations for their mosquito-repellent, resp. mosquitocide effect. All preparations are soluble in acetone; with exception of the 50% solution of Lauseto, they are all 100% (full strength):

1. Lauseto
2. Muth 2509/1
3. Muth 2567/1

5. Piepenbrink 3083
6. Piepenbrink 3084
7. Lober 3/340 b.

Eulan techn.

Under separate cover:  
7 small bottles

/s/ Dr. Drapal

\* \* \* \* \*

TO: Coleristic Department, attn: Dr. Drapal, Leverkusen  
17 Feb. 1944 Dr.Md./B. 3 April 1944

Re: Test for mosquito-repellent effect.

The 7 preparations mentioned in your letter have been tested in comparison to Cesarol for their mosquitocide effect. All substances were dissolved like Cesarol at 1% in ether, and they were used in this 1% solution in the impregnation of muslin for mosquito cages. 16 hrs. after this treatment the same number of mosquitoes (*Culex pipiens*) was placed in each cage and observed during the following hours. "Effect" signifies that at a certain point of time 70-100% of the mosquitoes were dead, while "slight trace effect" signifies that a number of the insects (70-80%) survived. 15-16 days later the same cages were examined once more in the same manner. Since the effect of Cesarol persisted still after 2 months, we shall test these substances which still show a mosquitocide effect after 2 weeks again after 1-2 months, and we shall inform you on the results. In the following I quote the results that were obtained until now:

Preparation	1st Test	2nd Test
	(16 hrs. after treatm.)	(15-16 days after treatm.)

Pb 460=Lauseto	after 5 hrs., effect	after 5 hrs., effect
Pb 461=Muth 2509/1	after 5 hrs., effect	after 6 hrs., effect
Pb 462=Muth 2567/1	after 4 hrs., effect	after 8 hrs., sl.tr. eff.-ø

Pb 463=Schweitzer		
50/181	after 2 hrs., effect	after 8 hrs., ø

Pb 464=Piepenbrink		
3083	after 3 hrs., effect	after 8 hrs., ø

Pb 465=Piepenbrink		
3084	after 5 hrs., effect	after 6 hrs., effect

Pb 466=Lober 3/340 b		
	after 2 hrs., effect	after 8 hrs., sl.tr. eff.-ø

Thus the preparations Pb 462, 463, 464, and 466 are eliminated from the tests.



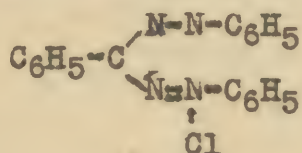
Heil Hitler!  
Chemotherapeutic Laboratory  
/s/ Dr. Lutter /s/ Dr. Mudrow

Ø Dir. Dr. Schönhöfer

I. G. FARBENINDUSTRIE AKTIENGESellschaft  
WERK ELBERFELD  
/s/ Dr. Schönhöfer ppa. Kikuth.

## A P P E N D I X 4

### Preparation of Triphenyltetrazoliumchlorid (Tetrazoliumsalz)



Zu 400 g Triphenylformazan  $\text{C}_6\text{H}_5-\text{C}-\begin{array}{l} \text{N}-\text{NH} \text{ C}_6\text{H}_5 \\ \quad \quad \diagdown \quad \diagup \\ \quad \quad \quad \text{N}=\text{N}-\text{C}_6\text{H}_5 \end{array}$ , 1,7 Ltr. Trockensprit

und 330 Amylnitrit lässt man in einem 3 Ltr.-Kolben unter Rühren 185 g 37% alkoholische Salzsäure zutropfen. Durch die Reaktionswärme steigt die Temperatur im Innern des Kolbens auf 50-55°. Wenn die alkoholische Salzsäure zuge- tropft ist, wird noch 1 1/2 - 2 Stunden nachgerührt, dann, ohne zu rühren, noch 4 Stunden stehen lassen, bis keine Blasenentwicklung (Stickstoff) mehr zu bemerken ist. Die rote Farbe des Triphenylformazans ist verschwunden und eine tiefbraune Lösung entstanden. Diese Lösung wird darauf solange mit Leitungswasser versetzt, bis sich deutlich eine Ölschicht (in der Hauptsache Amylalkohol) abscheidet, wozu ungefähr 6-8 Ltr. Wasser erforderlich sind. Die wässrig- alkohol. Lösung wird durch Ablassen von der Ölschicht getrennt und im Vakuum oder auf dem Wasserbad bis auf 1 - 1 1/2 Ltr. eingeeengt. Zur Klärung behandelt man noch heiss mit Tierkohle und saugt ab. Das gelbliche Filtrat wird jetzt auf dem Wasserbad bis zur beginnenden Krystallisation weiter eingedampft, auf Eis gestellt, wodurch das wasserhaltige Rohprodukt des Triphenyltetrazoliumchlorids in fester Form erhalten wird. Zwecks Reinigung wird das Rohprodukt in heissem Wasser gelöst (auf 1 Teil Rohprodukt höchstens 1 Teil Wasser). Die Lösung reagiert meist kongosauer, deshalb muss mit 20% Ammoniaklösung bis zum Verschwinden der kongo-

säuren Reaktion (aber noch deutlich lackmussauer!) abgestumpft werden, wozu ca. 30-40 ccm Ammoniaklösung erforderlich sind. Ausserdem wird nochmals etwas Tierkohle zugegeben und noch warm abgesaugt. Das Filtrat wird in Eiswasser gestellt und unter Umrühren zur Krystallisation gebracht. Man erhält dann ein fast farbloses Triphenyltetrazoliumchlorid, das abgesaugt zunächst 2 Tage lang bei gewöhnlicher Temperatur unter Ausschluss von Licht und dann erst im Dampfschrank getrocknet wird. Triphenyltetrazoliumchlorid stellt ein schwach gelb- bräunliches Krystallpulver dar, das bei 241° sich zersetzt und die erforderlichen Reinheitsprüfungen erfüllen muss. Ausbeute gegen 300 g = 67-68% d.Th.

### Darstellung von Benzyliden-phenylhydrazon.

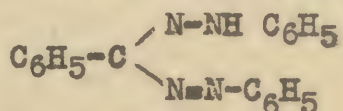
Zu 108 g Phenylhydrazin und 200 ccm Trockensprit lässt



man in einem 1 Ltr.-Kolben unter Rühren 106 g Benzaldehyd zutropfen. Wenn der Benzaldehyd zugegeben ist, wird 30 Min. lang gekocht; hierauf wird mit Eiswasser abgekühlt, das gebildete Benzyliden-phenylhydrazon abgesaugt und mit kaltem Trockensprit und etwas Aether nachgewaschen. Die Trocknung des Benzyliden-phenylhydrazons erfolgt im lichtgeschützten Exsiccator über Chlorkalzium, wobei man am besten im Wasserstrahlvakuum trocknet. Ausbeute 162 g gleich 83% der Th. Die getrocknete Substanz wird in braunen Flaschen aufgehoben.

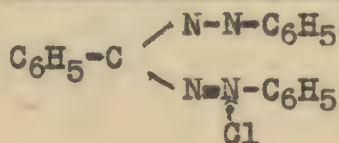
### Darstellung von Triphenylformazan.

77 g Anilin und 207 ccm Salzsäure conc. werden bei einer Temperatur, die + 10° nicht übersteigen soll, mit einer wässrigen Lösung von 59 g Natriumnitrit diazotiert. Die Diazolösung wird rasch filtriert. Während des Filtrierens oder schon vorher, hat man sich eine Lösung von 162 g Benzyliden-phenylhydrazon in 350 ccm Pyridinfraktion II und 350 ccm Trockensprit bereitet und diese Lösung in einem grossen Becherglas unter Rühren auf 15-20° heruntergekühlt. Dann lässt man bei dieser Temperatur die filtrierte Diazolösung unter Rühren zutropfen. Die Temperatur steigt bei dem Zutropfen der Diazolösung auf ca. 25°, was nicht schadet. Höhere Temperaturen sind jedoch durch Aussenkühlung mit Eis zu vermeiden. Um eine Zersetzung der Diazolösung hintanzuhalten, stellt man sie bis zur Verwendung in Eiswasser. Nach dem Zutropfen der Diazolösung wird noch mindestens 2 - 3 Stunden weiter gut durchgerührt; hierauf wird der entstandene rote Niederschlag, der das rohe Triphenylformazan darstellt. Formel:



abgesaugt und mehrmals mit Wasser gewaschen. Ausbeute 205 g. Zum Zweck der Weiterverarbeitung auf Triphenyltetrazoliumchlorid genügt es, das lufttrockene Triphenylformazan mit 15 Raumteilen Trockensprit auszukochen. Zu diesem Zweck werden beispielsweise 205 g des Triphenylformazans mit 3075 ccm Trockensprit 30-40 Min. lang gekocht, kalt über Nacht stehen lassen und schliesslich abgesaugt. Man erhält ein violettrot schimmerndes kristallisiertes Produkt, das den Sm. 170-173° aufweist und für die Weiterverarbeitung geeignet ist. Ausbeute: 80% des Rohproduktes = 164 g.

### Darstellung von Triphenyltetrazoliumchlorid (Tetrazoliumsalz)





Zu 400 g Triphenylformazan  $\text{C}_6\text{H}_5-\text{C} \begin{array}{l} \nearrow \text{N-NH C}_6\text{H}_5 \\ \searrow \text{N=N-C}_6\text{H}_5 \end{array}$ , 1,7 Ltr. Trockensprit

und 330 Amylnitrit lässt man in einem 3 Ltr.-Kolben unter Rühren 185 g 37% alkoholische Salzsäure zutropfen. Durch die Reaktionswärme steigt die Temperatur im Innern des Kolbens auf 50-55°. Wenn die alkoholische Salzsäure zugetropft ist, wird noch 1 1/2 - 2 Stunden nachgerührt, dann, ohne zu rühren, noch 4 Stunden stehen gelassen, bis keine Blasenentwicklung (Stickstoff) mehr zu bemerken ist. Die rote Farbe des Triphenylformazans ist verschwunden und eine tiefbraune Lösung entstanden. Diese Lösung wird darauf solange mit Leitungswasser versetzt, bis sich deutlich eine Ölschicht (in der Hauptsache Amylalkohol) abscheidet, wozu ungefähr 6-8 Ltr. Wasser erforderlich sind. Die wässrig-alkohol. Lösung wird durch Ablassen von der Ölschicht getrennt und im Vakuum oder auf dem Wasserbad bis auf 1 - 1 1/2 Ltr. eingeeengt. Zur Klärung behandelt man noch heiss mit Tierkohle und saugt ab. Das gelbliche Filtrat wird jetzt auf dem Wasserbad bis zur beginnenden Krystallisation weiter eingedampft, auf Eis gestellt, wodurch das wasserhaltige Rohprodukt des Triphenyltetrazoliumschlörds in fester Form erhalten wird. Zwecks Reinigung wird das Rohprodukt in heissem Wasser gelöst (auf 1 Teil Rohprodukt höchstens 1 Teil Wasser). Die Lösung reagiert meist kongosauer, deshalb muss mit 20% Ammoniaklösung bis zum Verschwinden der kongosäuren Reaktion (aber noch deutlich lackmussauer!) abgestumpft werden, wozu ca. 30-40 ccm Ammoniaklösung erforderlich sind. Ausserdem wird nochmals etwas Tierkohle zugegeben und noch warm abgesaugt. Das Filtrat wird in Eiswasser gestellt und unter Umrühren zur Krystallisation gebracht. Man erhält dann ein fast farbloses Triphenyltetrazoliumchlorid, das abgesaugt zunächst 2 Tage lang bei gewöhnlicher Temperatur unter Ausschluss von Licht und dann erst im Dampfschrank getrocknet wird. Triphenyltetrazoliumchlorid stellt ein schwach gelb-bräunliches Krystallpulver dar, das bei 241° sich zersetzt und die erforderlichen Reinheitsprüfungen erfüllen muss. Ausbeute gegen 300 g = 67-68% d.Th.

### Darstellung von Benzyliden-phenylhydrazon.

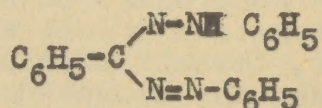
Zu 108 g Phenylhydrazin und 200 ccm Trockensprit lässt man in einem 1 Ltr.-Kolben unter Rühren 106 g Benzaldehyd zutropfen. Wenn der Benzaldehyd zugetropft ist, wird 30 Min. lang gekocht; hierauf wird mit Eiswasser abgekühlt, das gebildete Benzyliden-phenylhydrazon abgesaugt und mit kaltem Trockensprit und etwas Äther nachgewaschen. Die Trocknung des Benzyliden-phenylhydrazons erfolgt im lichtgeschützten Exiccator über Chlorkalzium, wobei man am besten im Wasserstrahlvakuum trocknet. Ausbeute 162 g gleich 83% der Th. Die



getrocknete Substanz wird in braunen Flaschen aufgehoben.

### Darstellung von Triphenylformazan.

77 g Anilin und 207 ccm Salzsäure conc. werden bei einer Temperatur, die + 10° nicht übersteigen soll, mit einer wässrigen Lösung von 59 g Natriumnitrit diazotiert. Die Diazolösung wird rasch filtriert. Während des Filtrierens oder schon vorher, hat man sich eine Lösung von 162 g Benzyliden-phenylhydrazon in 350 ccm Pyridinfraktion II und 350 ccm Trockensprit bereitet und diese Lösung in einem grossen Becherglas unter Rühren auf 15-20° heruntergekühlt. Dann lässt man bei dieser Temperatur die filtrierte Diazolösung unter Rühren zutropfen. Die Temperatur steigt bei dem Zutropfen der Diazolösung auf ca. 25°, was nicht schadet. Höhere Temperaturen sind jedoch durch Aussenkühlung mit Eis zu vermeiden. Um eine Zersetzung der Diazolösung hintanzuhalten, stellt man sie bis zur Verwendung in Eiswasser. Nach dem Zutropfen der Diazolösung wird noch mindestens 2 - 3 Stunden weiter gut durchgerührt; hierauf wird der entstandene rote Niederschlag, der das rohe Triphenylformazan darstellt. Formel:



abgesaugt und mehrmals mit Wasser gewaschen. Ausbeute 205 g. Zum Zweck der Weiterverarbeitung auf Triphenyltetrazoliumchlorid genügt es, das lufttrockene Triphenylformazan mit 15 Raumteilen Trockensprit auszukochen. Zu diesem Zweck werden beispielsweise 205 g des Triphenylsformazans mit 3075 ccm Trockensprit 30-40 Min. lang gekocht, kalt über Nacht stehen lassen und schliesslich abgesaugt. Man erhält ein violettrot schimmerndes krystallisiertes Produkt, das den Sm. 170-173° ausweist und für die Weiterverarbeitung geeignet ist. Ausbeute: 80% des Rohproduktes = 164 g.





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